



SEQUENCE LISTING

<110> Korman, Allen
Halk, Edward L.
Lonberg, Nils
Medarex, Inc.

<120> Human CTLA-4 Antibodies and Their Uses

<130> 014643-010510US

<140> US 09/644,668

<141> 2000-08-24

<150> US 60/150,452

<151> 1999-08-24

<160> 41

<170> PatentIn Ver. 2.1

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<223> Description of Artificial Sequence:cloning vector
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<223> preliminary sequence for heavy chain fragment
10D1.3

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attcaccatc tccagagaca attccaagaa cacgctgtat ctgcaaatga acagcctgag 240
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<210> 3

<211> 321

<212> DNA

<213> Homo sapiens

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<223> preliminary sequence for light chain fragment
10D1.3

<400> 3

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ggctcgggac agacttcact ctcaccatca gcagactgga gcctgaagat tttgcagtgt 240
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<210> 4
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<220>
 <223> Vk A-27 germline sequence

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 cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180
 gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240
 cctgaagatt ttgcagtgtg ttactgtcag cagtatggta gctcacc 287

<210> 5
 <211> 95
 <212> PRT
 <213> Homo sapiens

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 <223> light chain variable region predicted sequence for
 Vk A-27 germline

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 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
 20 25 30
 Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
 35 40 45
 Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
 50 55 60
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
 65 70 75 80
 Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser
 85 90 95

<210> 6
 <211> 325
 <212> DNA
 <213> Homo sapiens

<220>
 <223> light chain variable region (Vk), 10D1 from Vk
 A-27

<400> 6
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 gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240
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 caagggacca aggtggaaat caaac 325

<210> 7
 <211> 108
 <212> PRT
 <213> Homo sapiens

<220>
 <223> light chain variable region predicted sequence for
 10D1 from Vk A-27

<400> 7
 Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Ser Ser
 20 25 30
 Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
 35 40 45
 Ile Tyr Gly Ala Phe Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
 50 55 60
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
 65 70 75 80
 Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
 85 90 95
 Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 8
 <211> 325
 <212> DNA
 <213> Homo sapiens

<220>
 <223> light chain variable region (Vk) 4B6 from Vk A-27

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 cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180
 gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240
 cctgaagatt ttgcagtgtg ttactgtcag cagtatggta gctcaccgtg gacgttcggc 300
 caagggacca aggtggaaat caaac 325

<210> 9
 <211> 108
 <212> PRT
 <213> Homo sapiens

<220>
 <223> light chain variable region predicted sequence for
 4B6 from Vk A-27

<400> 9

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
 20 25 30
 Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
 35 40 45
 Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
 50 55 60
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
 65 70 75 80
 Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
 85 90 95
 Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 10
 <211> 287
 <212> DNA
 <213> Homo sapiens

<220>
 <223> Vk L-15 germline sequence

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 gaagattttg caacttatta ctgccaacag tataatagtt accctcc 287

<210> 11
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 <212> PRT
 <213> Homo sapiens

<220>
 <223> light chain variable region predicted sequence for
 Vk L-15 germline

<400> 11
 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
 20 25 30
 Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
 35 40 45
 Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

<223> VH 3-30.3 germline sequence

<400> 14

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ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagcaa taaatactac 180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaga      294
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<210> 15

<211> 98

<212> PRT

<213> Homo sapiens

<220>

<223> heavy chain variable region predicted sequence for
VH 3-30.3 germline

<400> 15

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  1                      5                      10                      15
```

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
                20                      25                      30
```

```
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
    35                      40                      45
```

```
Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50                      55                      60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
    65                      70                      75                      80
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```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                      90                      95
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Ala Arg

<210> 16

<211> 355

<212> DNA

<213> Homo sapiens

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<223> heavy chain variable region VH 10D1 from VH 3-30.3

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ctgcaaatga acagcctgag agctgaggac acggctatat attactgtgc gaggaccggc 300
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<210> 17

<211> 118

<212> PRT
 <213> Homo sapiens

<220>
 <223> heavy chain variable region predicted sequence for
 10D1 from VH 3-30.3

<400> 17
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 1 5 10 15
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 20 25 30
 Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Thr Phe Ile Ser Tyr Asp Gly Asn Asn Lys Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
 85 90 95
 Ala Arg Thr Gly Trp Leu Gly Pro Phe Asp Tyr Trp Gly Gln Gly Thr
 100 105 110
 Leu Val Thr Val Ser Ser
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<210> 18
 <211> 355
 <212> DNA
 <213> Homo sapiens

<220>
 <223> heavy chain variable region VH 4B6 from VH 3-30.3

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<210> 19
 <211> 118
 <212> PRT
 <213> Homo sapiens

<220>
 <223> heavy chain variable region predicted sequence for
 4B6 from VH 3-30.3

<400> 19
 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg


```

      1             5             10             15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
      20             25             30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
      35             40             45
Thr Phe Ile Ser Tyr Asp Gly Ser Asn Lys His Tyr Ala Asp Ser Val
      50             55             60
Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
      65             70             75             80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
      85             90             95
Ala Arg Thr Gly Trp Leu Gly Pro Phe Asp Tyr Trp Gly Gln Gly Thr
      100            105            110
Leu Val Thr Val Ser Ser
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<210> 20

<211> 296

<212> DNA

<213> Homo sapiens

<220>

<223> VH 3-33 germline sequence

<400> 20

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gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
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<210> 21

<211> 98

<212> PRT

<213> Homo sapiens

<220>

<223> heavy chain variable region predicted sequence for
VH 3-33 germline

<400> 21

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  1             5             10             15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
      20             25             30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
      35             40             45
Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
      50             55             60

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Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg

<210> 22
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 <223> heavy chain variable region VH 1E2 from VH 3-33

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 gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
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<220>
 <223> heavy chain variable region predicted sequence for
 1E2 from VH 3-33

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 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Phe Tyr Cys
 85 90 95

Ala Arg Ala Pro Asn Tyr Ile Gly Ala Phe Asp Val Trp Gly Gln Gly
 100 105 110

Thr Met Val Thr Val Ser Ser
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<210> 24
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 <213> Homo sapiens

<220>
 <223> light chain CDR1 (HuMab 10D1)

<400> 24
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<210> 25
 <211> 12
 <212> PRT
 <213> Homo sapiens

<220>
 <223> light chain CDR1 (HuMab 4B6)

<400> 25
 Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu Ala
 1 5 10

<210> 26
 <211> 11
 <212> PRT
 <213> Homo sapiens

<220>
 <223> light chain CDR1 (HuMab 1E2)

<400> 26
 Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala
 1 5 10

<210> 27
 <211> 5
 <212> PRT
 <213> Homo sapiens

<220>
 <223> heavy chain CDR1 (HuMab 10D1, 4B6)

<400> 27
 Ser Tyr Thr Met His
 1 5

<210> 28
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<220>
 <223> heavy chain CDR1 (HuMab 1E2)

<400> 28
 Ser Tyr Gly Met His
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<210> 29
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<220>
 <223> light chain CDR2 (HuMab 10D1)

<400> 29
 Gly Ala Phe Ser Arg Ala Thr
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<210> 30
 <211> 7
 <212> PRT
 <213> Homo sapiens

<220>
 <223> light chain CDR2 (HuMab 4B6)

<400> 30
 Gly Ala Ser Ser Arg Ala Thr
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<210> 31
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<220>
 <223> light chain CDR2 (HuMab 1E2)

<400> 31
 Ala Ala Ser Ser Leu Gln Ser
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<210> 32
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<220>
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<400> 32
 Phe Ile Ser Tyr Asp Gly Asn Asn Lys Tyr Tyr Ala Asp Ser Val Lys
 1 5 10 15

Gly

<210> 33
 <211> 17
 <212> PRT
 <213> Homo sapiens

<220>
 <223> heavy chain CDR2 (HuMab 4B6)

<400> 33
 Phe Ile Ser Tyr Asp Gly Ser Asn Lys His Tyr Ala Asp Ser Val Lys
 1 5 10 15

Gly

<210> 34
 <211> 17
 <212> PRT
 <213> Homo sapiens

<220>
 <223> heavy chain CDR2 (HuMab 1E2)

<400> 34
 Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys
 1 5 10 15

Gly

<210> 35
 <211> 9
 <212> PRT
 <213> Homo sapiens

<220>
 <223> light chain CDR3 (HuMab 10D1, 4B6)

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<210> 36
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<220>
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<213> Homo sapiens

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<223> heavy chain CDR3 (HuMab 10D1, 4B6)

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<210> 39

<211> 506

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence:kappa light
chain plasmid pCK7-96 (partial)

<400> 39

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<212> DNA

<213> Artificial Sequence

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chain plasmid pCG-96

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<212> DNA

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